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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/051,727	01/17/2002	Rebanta Bandyopadhyay	LD0189 NP	8647

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EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	
ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 07/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/051,727	BANDYOPADHYAY ET AL.	
	Examiner	Art Unit	
	Lakshmi S Channavajjala	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-29 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 1-29 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt of declaration & fee dated 4-22-02 and IDS dated 4-16-02 is acknowledged.

Claims 1-29 are pending.

Claims 1-14, 18-23 are directed to a process of formulating an epothilone analogue for parenteral administration comprising the steps of dissolving epothilone analogues in tert-butanol, drying under vacuum to form a lyophilized product, followed by a second drying and packaging the lyophilized product in a vial containing an equal mixture of a nonionic surfactant and anhydrous ethanol.

Claims 15-17 are directed to a pharmaceutical composition containing lyophilized epothilone analog claimed.

Claims 24-29 are directed a process for treating a patient in need of treatment with a composition of claims 18-20.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

1. Claims 1-29 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-29 of copending Application No. 10/055,653 (US Pub. No.

2002/0169190 A1). This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1-29 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 30-91 of copending Application No. 10/055,653 (US Pub. No. 2002/0169190 A1) in view of US 4,950,432 to Mehta et al. The scope of instant claims directed to a process of treating a patient in need thereof with the epitholine containing composition includes the condition i.e., cancer, of the copending claims. Further, both the sets of claims recite the same epothilone analogue, surfactant and recite parenteral administration. Copending claims do not recite lyophilized epothilone analog.

Mehta et al teach liposomal powders of macrolide antibiotics prepared by by dissolving the compound in a series of solvents, evaporation, dissolving in a mixture of tert-butanol and methylene chloride followed by filtration and lyophilization. Mehta teaches producing a stable

macrolide composition that is suitable for systemic administration by lyophilization. Therefore, it would have been obvious for one of an ordinary skill in the art to prepare a lyophilized product by employing the steps of Mehta et al because Mehta et al teach lyophilization results in a stable product that can be stored for a long time and that is suitable for systemic administration. Thus, one of an ordinary skill in the art would have recognized that lyophilization of a macrolide compound (such as epothilone of instant claims) would render the compound stable and reduces its hydrophobicity making it suitable for systemic administration.

This is a provisional obviousness-type double patenting rejection.

3. Claims 15-29 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-52 of U.S. Patent No. 6,576,651 B2 in view of US 4,950,432 to Mehta et al. Instant claims directed to a pharmaceutical composition containing epothilone analog and a process of treating a patient in need thereof with the epitholine containing composition. Instant claims recite "for parenteral administration" which is in an intended use. Patented claims recite the same epothilone analogues, however recites in an oral compositions. The patented claims do not recite lyophilized epothilone analog.

Mehta et al teach liposomal powders of macrolide antibiotics prepared by dissolving the compound in a series of solvents, evaporation, dissolving in a mixture of tert-butanol and methylene chloride followed by filtration and lyophilization. Mehta teaches producing a stable macrolide composition that is suitable for systemic administration by lyophilization. Therefore, it would have been obvious for one of an ordinary skill in the art to prepare a lyophilized product by employing the steps of Mehta et al because Mehta et al teach lyophilization results in a stable

product that can be stored for a long time and that is suitable for systemic administration. Thus, one of an ordinary skill in the art would have recognized that lyophilization of a macrolide compound (such as epothilone of instant claims) would render the compound stable and reduces its hydrophobicity making it suitable for systemic administration.

Claim Rejections - 35 USC § 103

Claims 1-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,380,395 to Vite et al (Vite) in view of US 4,950,432 to Mehta et al (Mehta).

Vite teaches epothilone derivatives for treating carcinomas, tumors, and a variety of human diseases (col. 5). The compounds of Vite read on the instant epothilone compounds (cols. 1-3). Vite teaches formulating the compounds for oral, intravenous and other routes of administration in the form of powders, solutions etc (col. 6). However, Vite does not teach the claimed lyophilization steps and reconstituting epothilone analog.

Mehta et al teaches macrolide antibiotics such as nystatin and amphotericin B and their encapsulation in to liposome for administration to the patient (col. 4). Mehta et al teaches that most of the macrolide antibiotics are limited by their hydrophobicity that precludes its systemic administration and therefore are administered only orally. Mehta et al teaches preparing liposome encapsulated macrolide antibiotics comprising the steps of dissolving phospholipids and antibiotics in solvents such as tert-butanol, methylene chloride, filtering and freezing the resultant mixture and finally lyophilization to produce a powder. It would have been obvious for one of an ordinary skill in the art at the time invention to prepare epothilone derivatives encapsulated in liposome using the procedure of Mehta et al i.e., involving lyophilization steps to

obtain a final powder and reconstitute the powders using desired solvents because Mehta et al teach macrolide antibiotics prepared by the above method are suitable for systemic administration and are stable for extended periods. Examiner notes that instant applicants also achieve the same stability by lyophilization of instant epothilone compounds (page 13, lines 10-15). Mehta et al does not teach instant epothilone analog or the exact steps of lyophilization claimed or the claimed Lactated Ringer's injection. However, choosing the suitable or appropriate temperature and pressure condition for the process of lyophilization by routine optimization would be within the scope of a skilled artisan. Further, using the appropriate diluents such the claimed Lactated Ringer's for intravenous is within the scope of a skilled artisan.

Specification

The use of the trademark Taxol and Cremophor has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

Claims 18-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 18, 19 and 20 the phrases "any of claim 15", "any of claim 16" and "any of claim 17" respectively are vague and indefinite because it is unclear from the claims as to what is being referred to in an alternate form in the claims. If is with respect to the composition, the independent claims from which these claims depend do not recite compositions in plural and only recite one composition.

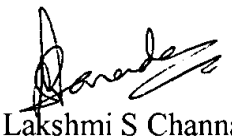
Information Disclosure Statement

Examiner has not considered references AA and AC because the reference AA is a US application that has been abandoned and reference AC is a provisional application, not a US patent.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S Channavajjala whose telephone number is 703-308-2438. The examiner can normally be reached on 7.30 AM -4.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-7924 for regular communications and 703-308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.



Lakshmi S Channavajjala
Examiner
Art Unit 1615
July 26, 2003